FDA Public Health Web Notification*: Information for Physicians on Sub-acute Thromboses (SAT) and Hypersensitivity Reactions with Use of the Cordis CYPHER™ Coronary Stent

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Why is the Food and Drug Administration (FDA) issuing this notification?

Shortly after the April 24, 2003, approval of the Cordis CYPHER™ Coronary Stent, we began receiving adverse event reports through the Medical Device Reporting (MDR) system. We are still analyzing the information contained in these reports, but wanted to share with you the information we have at this time and encourage you to report your experience (see instructions and links below).

What is the CYPHER™ stent?

The CYPHER™ stent is a coronary stent coated with a thin polymer containing the drug sirolimus. The CYPHER™ stent releases an immunosuppressant drug, sirolimus, intended to reduce restenosis. For more information on the CYPHER™ stent, see the physician Instructions for Use at http://www.fda.gov/cdrh/pdf3/P020026c.pdf or the patient guide at http://www.fda.gov/cdrh/pdf3/P020026d.pdf. For more information on the drug sirolimus, which is marketed as Rapamune™, see the physician Instructions for Use at www.fda.gov/cder/foi/label/2003/021083s006lbl.pdf.

What information is being reported?

We have received numerous reports of adverse events for the CYPHER™ stent through our MDR system, which is subject to significant underreporting. As of October 20, 2003, we have received more than 290 reports (>260 US and >25 Outside US) involving sub-acute (occurring between 24-hours and 30 days post-procedure) thrombosis (SAT) associated with the CYPHER™ stent. More than 60 reports of SATs were associated with patient death and the remaining reports were associated with patient injury requiring medical or surgical intervention. Also, we have received more than 50 reports, including some deaths, that Cordis considers possible hypersensitivity reactions. The symptoms reported include: pain, rash, respiratory alterations, hives, itching, fever, and blood pressure changes. We do not have sufficient data to establish rates for these events, nor can we determine whether these rates are different from those experienced with bare metal stents.

* CDRH Web Notifications are intended to augment the existing Safety Notification program by providing a mechanism to quickly disseminate device–related safety information that may be beneficial to healthcare providers. Unlike other forms of Notifications, such as Safety Alerts or Public Health Advisories, Web Notifications usually do not make specific recommendations and are typically used in situations where the available information and our understanding of an issue are still evolving.

As of October 10, 2003, Cordis reports that more than 450,000 units have been distributed worldwide (>260,000 US and >180,000 Outside US).

What are FDA and Cordis doing about the SATs and hypersensitivity reactions?

After receiving a number of reports of thrombotic events, Cordis, in conjunction with FDA, issued a letter on July 7, 2003 (see http://www.fda.gov/bbs/topics/NEWS/2003/NEW00919.html) reminding physicians to follow the instructions for use and to report any adverse events to the Agency.

FDA and Cordis are gathering as much information as we can about the circumstances surrounding both SATs and hypersensitivity reactions. FDA is also working with the regulatory bodies of other countries to gain more information about foreign experience with the product.

What is causing these events?

While the etiology of reported adverse events associated with the CYPHER™ stent has not been identified, we are exploring a number of possibilities. We do not know whether product characteristics, patient characteristics (e.g. concomitant medications or illnesses), procedural factors, or a combination of these may have contributed to the events.

What can be done to reduce the likelihood that an SAT or hypersensitivity reaction will occur?

Until we can identify the cause(s) of the events, we cannot make specific recommendations. As we learn more about the mechanisms for these events, we will share that information with you. We do encourage you to follow the instructions for use.

Because of the uncertainty of the cause of reported hypersensitivity reactions, we urge you to be vigilant for any patient symptom that may be attributed to hypersensitivity.

In the meantime, we would like your help in gathering more information about these types of events. Historically, underreporting has made it difficult for FDA to properly assess the incidence of adverse events. You can help us by following your facility reporting procedures as noted below. We also appreciate any voluntary reports submitted by clinicians and patients.

How do I report adverse events to FDA?

The Medical Device Reporting (MDR) regulation, 21 CFR Part 803, requires hospitals and other user facilities, as defined by Part 803.3, to report adverse events to FDA and the device manufacturer when the event is associated with the use of the medical device and the device may have caused or contributed to a patient death or serious injury. You may refer to our MDR web site at: http://www.fda.gov/cdrh/mdr.

You can also report to MedWatch, the FDA's voluntary reporting program. You may submit reports to MedWatch one of four ways: online at

http://www.accessdata.fda.gov/scripts/medwatch/; by telephone at 1-800-FDA-1088; by FAX at 1-800-FDA-0178; or by mail to MedWatch, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

FDA Contacts

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Additionally, a voice mail message may be left at 301-594-0650 and your call will be returned as soon as possible.